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In this issue, we offer a 'Rapid Communication' on why the Ebola outbreak in West Africa has been so challenging to control. Also, estimates suggest that each year about 1 in 8 Canadians (4 million people) get sick from the food they eat – find out how outbreaks of food-borne illness in Canada are managed once they have been clinically diagnosed and reported to public health. Finally, catch up with the most recent statements by the National Advisory Committee on Immunization (NACI).

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Why has the Ebola outbreak in West Africa been so challenging to control?

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Abstract

West Africa is in the midst of the largest Ebola outbreak ever; there have been over 1000 deaths and many new cases are reported each day. The World Health Organization (WHO) declared it an outbreak in March 2014 and on August 6, 2014 the WHO declared the outbreak a public health emergency of international concern. Based on the number of deaths and total number of cases reported to the WHO as of August 11, 2014, the current outbreak has an overall mortality rate of 55%. Outbreak control measures against Ebola virus disease are effective. Why then, has this outbreak been so challenging to control? Ebola is transmitted through bodily fluids and immediately attacks the immune system, then progressively attacks the major organs and the lining of blood vessels. Sierra Leone, Guinea and Liberia are small countries that have limited resources to respond to prolonged outbreaks, especially in rural areas. This has been made more challenging by the fact that health care workers are at risk of contracting Ebola virus disease. Treatment to date has been supportive, not curative and outbreak control strategies have been met with distrust due to fear and misinformation. However, important progress is being made. The international response to Ebola is gaining momentum, communication strategies have been developed to address the fear and mistrust, and promising treatments are under development, including a combination of three monoclonal antibodies that has been administered to two American Ebola-infected health care workers. The National Microbiology Laboratory of the Public Health Agency of Canada (PHAC) has been supporting laboratory diagnostic efforts in West Africa and PHAC has been working with the provinces and territories and key stakeholders to ensure Canada is prepared for a potential Ebola importation.

Introduction

Four West African countries are in the midst of the largest Ebola outbreak the world has seen. The World Health Organization (WHO) declared it an outbreak in March 2014. On August 6, 2014, the WHO, based on the recommendations of its Emergency Committee, declared the current outbreak a Public Health Emergency of International Concern (PHEIC) (1). As of August 11, 2014, the WHO has reported 1848 cases and 1013 deaths in Guinea, Sierra Leone, Liberia and Nigeria (1). Based on these reported deaths and total number of cases, this outbreak currently has an overall mortality rate of 55%.

The objective of this article is to summarize what we know about Ebola virus disease, current challenges to controlling the outbreak, and progress to date, including Canada's contribution to the outbreak response.

Background

Ebola belongs to the family Filoviridae, in which most members cause severe hemorrhagic fever in humans. There are five species: *Zaire ebolavirus*, *Sudan ebolavirus*, *Bundibugyo ebolavirus*, *Tai forest ebolavirus*, and *Reston ebolavirus*. Each species contains one virus (Table 1) (2, 3).

Table 1: Species of Genus *Ebolavirus* (3, 4)

Species	Virus	Region	Fatality Rate
<i>Zaire ebolavirus</i>	EBOV	Africa	60-90%
<i>Sudan ebolavirus</i>	SUDV	Africa	40-60%
<i>Bundibugyo ebolavirus</i>	BDBV	Africa	25%, based on one outbreak
<i>Tai forest ebolavirus</i>	TAFV	Africa	Unknown, only one known infection in Ivory Coast
<i>Reston ebolavirus</i>	RESTV	Asia	Not known to cause lethal infections in humans. Lethal in non-human primates.

The current outbreak is caused by a new variant of EBOV, the species most virulent in humans (5).

The natural reservoir of EBOV is unknown, but is thought to be fruit bats (6). EBOV is known to cause disease in humans, non-human primates, and other mammals (4, 7). EBOV is thought to enter the human population through exposure to the bodily fluids of an infected fruit bat or mammal, especially non-human primates. Human infection with EBOV has been associated with hunting and processing bushmeat (8-10).

Following an incubation period of 2 to 21 days, Ebola initially presents with non-specific symptoms (e.g. headaches, fever, and muscle pain). This progresses to a rash, diarrhea and vomiting typically followed by multi-organ failure, hemorrhaging and death. Person-to-person transmission occurs through direct contact with the bodily fluids and tissues of an infected person (2). Those most at risk of infection during outbreaks are family members and caregivers of infected individuals, individuals in contact with dead bodies during funeral preparations and rituals, and health care personnel through safety protocol breaches (e.g. needlestick injury) (11).

Although treatment options to date have been limited, outbreak control measures are effective in arresting transmission when they can be executed properly. These measures include barrier and quarantine methods to limit exposure, early identification, isolation of cases, contact tracing, communication strategies to decrease risky behaviours, and epidemiologic surveillance (11, 12, 13).

Outbreak control measures for Ebola are effective. Why then, has the West Africa outbreak been so challenging to control?

The Challenges

The Ebola virus has deadly attack mechanisms

The Ebola virus enters the host through small skin lesions and mucosal surfaces facilitated by its surface glycoprotein (GP). Upon cell entry, the virus replicates and, as progeny virus buds from the host cell membrane, the infected cell is destroyed (14, 15, 16). Analysis of tissues from infected human and non-human primates have demonstrated that viral replication occurs initially in leukocytes, epithelial cells, hepatocytes, splenic, adrenal cortical, and endothelial cells (4).

Leukocytes

Leukocytes – macrophages, monocytes and dendritic cells – are the primary cell targets of infection (17); this has a profound effect on the immune response. Macrophages and monocytes are part of the innate immune response and the body's first line of defense against infections. Cell death of monocytes and macrophages lead to a massive release of cytokines, thus attracting more macrophages to be infected (18, 19, 20). This causes a positive feedback loop between macrophages and cytokines which can lead to a dysregulated inflammatory response or cytokine storm (3, 19, 20, 23).

The death of infected dendritic cells means they are incapable of activating the adaptive immune response. Patients with fatal Ebola virus disease show almost no viral antigen specific antibodies due to suppressed B- and T-cell immunity (21). This is caused by anti-inflammatory cytokines released by macrophages, such as interleukin-10 (IL-10) (22). Thus, EBOV hyperstimulates the innate immune response and suppresses the adaptive immune response.

Epithelial, hepatic, splenic and adrenal cells

Infected leukocytes are thought to spread the virus systemically through the lymphatic system and blood. The virus then preferentially attacks epithelial, hepatic, splenic and adrenal cells (4). Infected epithelial cells lining the gut cause gastrointestinal symptoms during the early stages of infection (e.g. vomiting and diarrhea) (4). Infected hepatocytes lead to increased liver enzyme levels and impaired liver function. This may decrease the synthesis of coagulation factors, contributing to coagulation abnormalities (24). Infected splenic cells can lead to necrosis and hemorrhage into the abdominal cavity. Necrosis of adrenal cortical cells affects the regulation of blood pressure, and appears to contribute to septic shock during the later stages of infection (25). The virus eventually reaches all vital organs, leading to progressive organ failure and shock (4, 20).

Endothelial cells

Endothelial cells lining the blood vessels are targeted during later stages of infection. Endothelial impairment is thought to increase vascular permeability that can lead to hemorrhage, a prominent feature of infection in approximately 40-50% of patients (5, 14).

How this pathology links with clinical signs and symptoms are highlighted in **Table 2**.

Table 2: Pathophysiology and clinical signs and symptoms of Ebola virus infection

	Clinical signs and symptoms	Pathophysiology
Early symptoms	Abrupt onset of fever, chills, malaise, myalgia Severe sore throat	Infected monocytes and macrophages release cytokines
First week	Systemic: Prostration, lethargy	Cytokines contribute to systemic symptoms
	Gastrointestinal: Anorexia, nausea, vomiting, abdominal pain, diarrhea (and progressively bloody diarrhea and hematemesis)	Viral replication in epithelial and endothelial cells lead to gastrointestinal symptoms and bleeding
	Cardiac: Chest pain dyspnea, shortness of breath, cough, nasal discharge	Viral replication and necrosis in cardiac tissues
	Splenic: Fever, abdominal pain, hemorrhage, if rupture into peritoneal cavity	Viral replication and necrosis
	Hepatic: Elevated liver enzymes and coagulation abnormalities	Liver cells are infected leading to cell death and affecting clotting factor production
	Vascular: Conjunctival injection, postural hypotension, edema	Endothelial cells are taken over and cytokines released, leading to increased vascular permeability
	Neurologic: Headache, confusion, encephalitis, seizure, coma	Viral replication in brain tissue and vascular dysfunction
	Skin: Maculopapular rash with varying degrees of erythema and desquamation	Endothelial leakage

	Clinical signs and symptoms	Pathophysiology
Complications	Hemorrhage Petechiae, ecchymoses, uncontrolled bleeding from venipuncture sites, epistaxis, visceral hemorrhagic effusions and other mucosal hemorrhages	Infected hepatic cells result in elevated liver enzymes and coagulation abnormalities Damaged endothelial cells lead to increased vascular permeability
	Shock and hypotension Severe metabolic disturbances Disseminated intravascular coagulation and hypovolemic shock	Direct viral damage of tissues and organs may lead to organ failure and shock. Infected adrenal cells fail to regulate blood pressure, resulting in hypotension and septic shock. Diffuse coagulopathy
Laboratory findings	Early leucopenia, lymphopenia and subsequent neutrophilia, thrombocytopenia, prolonged prothrombin and partial thromboplastin times High serum aminotransferase levels Hyperproteinemia and proteinuria	Infected dendritic cells impair immune response Uncontrolled upregulation of cytokines and chemokines (cytokine storm) Widespread viral replication and cell death in spleen, kidney, liver, gonads, etc.

Elimination of the reservoir is not feasible

The prevalence and extent of the EBOV reservoir amongst wild animals is unknown, so sporadic cases of transmission from animals to humans cannot be prevented.

Treatment is supportive, not curative

There are currently no approved therapeutic treatments for Ebola. Until recently, treatment focused on rehydration, electrolyte management, antibiotics and antivirals to treat secondary infections and medications to control pain, fever and gastrointestinal distress (2).

The outbreak has reached urban areas

Historically, Ebola virus disease has been responsible for smaller outbreaks in the remote forests of Sub-Saharan Africa that have typically involved animal to human transmission and sporadic human to human transmission. This outbreak marks the first time EBOV has appeared in a capital city and has been imported by an infected person into Africa's most populous country, Nigeria. The unprecedented size and location of the outbreak, combined with the fact that the virus is now circulating in densely populated urban centers, sets up the conditions for sustained human-to-human transmission, making the outbreak even more challenging to control (1).

Affected countries have challenges in health care infrastructure

Sierra Leone, Guinea and Liberia are small countries that have limited resources to respond to prolonged outbreaks, especially in rural areas. This is the first time that West Africa has had to deal with an EBOV outbreak, therefore most primary health workers did not have any prior experience dealing with this virus. Limited surveillance and reporting systems may have delayed outbreak identification and the subsequent global response. The WHO has identified these issues as gaps in the outbreak response (1, 26).

Health care workers are at risk of infection

The WHO has reported health-facility transmission as a central issue during the current outbreak (1). Health care workers are at risk of contracting EBOV while caring for infected patients through accidental exposure to infected bodily fluids. To date, more than 170 health care workers have been infected and at least 81 have died (27).

These deaths have discouraged some health care workers and international organizations from participating in treatment and control efforts (1).

Outbreak control strategies have been met with distrust

Persistent community resistance has been identified as a major challenge in the health sector response to the outbreak (1). Effective prevention and control strategies have been undermined by fear, mistrust and misinformation within affected communities, leading some to believe that medical staff have brought the virus to the country. This has resulted in people refusing to cooperate with medical personnel, helping patients escape isolation wards, and exhibiting hostile behaviour (1, 26, 28). Traditional burial practices also pose a major risk to close relatives, since they typically involve the cleaning and rubbing of dead bodies that may have a high load of Ebola virus. The recommendation that these burial practices be performed by outbreak response team members has been perceived to conflict with beliefs and cultural practices (26).

Progress to date

The international response is building momentum

International aid and resources have been increasingly directed to West Africa to control the EBOV outbreak. The WHO has coordinated efforts to scale up the human and financial resources necessary to effectively conduct infection prevention and control activities and to implement infrastructure needed to manage future outbreaks, such as strengthening the surveillance and laboratory capacities. Numerous non-governmental organizations, including Médecins Sans Frontières, Save the Children, and religious organizations have been working on the ground to help stop the spread of this disease (1).

Based on the deliberations of an Emergency Committee, the WHO Director General has made a number of recommendations, including: affected states should declare the outbreak a national emergency and establish an emergency operation centre to coordinate support and response efforts; exit screening be conducted at all international airports, seaports and major land crossings to identify individuals with unexplained febrile illness; appropriate contact management; and all states should enhance their capacity to detect, investigate and manage Ebola cases through improved surveillance, laboratory diagnostic support and rapid response (29).

Canada has joined other nations, organizations, and the WHO by providing financial and technical support. As of August 8, 2014, Canada has contributed over \$5 million towards humanitarian, infection control and security interventions in West Africa (30). As a member of the WHO Global Outbreak Alert and Response Network (GOARN), Canada provides technical and human resources towards the identification and response to significant international outbreaks (31).

The National Microbiology Laboratory (NML) of the Public Health Agency of Canada (PHAC) has worked closely with the WHO to provide rapid diagnostic support in a mobile laboratory in Sierra Leone (32).

Within Canada, PHAC is taking the lead on national preparedness for Ebola cases, working closely with the provinces and territories and all affected stakeholders. Case definitions, infection control guidelines, public health management of cases and contacts associated with Ebola virus disease, environmental decontamination, biosafety guidelines and more are currently being updated. The Agency is also facilitating the development of specific clinical care guidelines with the Association of Medical Microbiology and Infectious Disease Canada, the Canadian Critical Care Society, and the Canadian Association of Emergency Physicians.

Communication strategies are being implemented to address fears and misconceptions

An assessment of the current outbreak led by Dr. Luis Sambo, the WHO Regional Director for Africa, has recommended that affected governments scale up national resources to promote behavioural change while respecting cultural practices (1). Local collaborations (e.g. training community members to identify contacts, and working with local leaders to effectively disseminate the correct information on EBOV) are being used to dispel misconceptions and strengthen control strategies (26). Collaborations with religious, community and tribal leaders are being used to disseminate information (26, 28). These messages are also being spread by television and radio (33).

Investigational therapies are under development

Several experimental treatments are currently under development (2, 34). Two infected Americans received an experimental drug, which contains three monoclonal human-mouse chimeric antibodies manufactured in the plant *Nicotiana benthamiana* (35). These antibodies demonstrated 100% protection against EBOV in infected cynomolgus macaques (36).

Another investigational treatment uses small interfering RNAs specific to certain EBOV genes to inhibit virus replication. A study demonstrated 66% and 100% protection from EBOV in macaques after four and seven post-exposure treatments, respectively (37).

Several experimental vaccines have also shown promise against EBOV in nonhuman primates, including an adenovirus-based and a vesicular stomatitis virus (VSV)-based vaccine. For example, the VSV-based vaccine has demonstrated high protective efficacy against EBOV disease, with an absence of noticeable adverse events in non-human primates (38-40). Discussions are ongoing about fast tracking both the adenovirus and the VSV based Ebola vaccines for Phase 1 clinical trials.

The use of experimental treatments on two Americans infected with EBOV has led to a WHO-hosted discussion on the ethical considerations of including such treatments in the response efforts (1, 41).

Conclusion

There are a number of factors that make the Ebola virus outbreak in West Africa a challenge to control. The EBOV has efficient ways to paralyze host defence mechanisms and attack vital organs. It resides in a poorly understood wildlife reservoir and has emerged in countries that have challenges in both health care capacity and risk communication. All these factors have occurred in the context of increasing global travel.

Canada has been an integral part of the global response through sending money, providing laboratory support, developing a vaccine and post exposure treatment, and collaborating internationally. The Public Health Agency of Canada will continue to work with its partners and coordinate the national response to enable the optimal detection, investigation, management and reporting of any potential cases of EBOV within Canada.

The WHO has identified the Ebola outbreak as a public health emergency of international concern. This will continue to require national and international collaboration and the ongoing vigilance of front line health care and public health professionals to end the outbreak in West Africa and prevent its global spread.

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Estimating the burden of food-borne illness in Canada

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Abstract

The Public Health Agency of Canada estimates that each year about 1 in 8 Canadians (4 million people) get sick from the food they eat. Four pathogens cause about 90% of the 1.6 million illnesses caused by known pathogens: *Norovirus* (1 million cases), *Clostridium perfringens* (177,000 cases), *Campylobacter* (145,000 cases) and nontyphoidal *Salmonella* (88,000 cases). These estimates are based on multiple complementary disease surveillance systems and the peer-reviewed literature. Understanding the burden of food-borne illness is useful for decision-makers, supporting the development of food safety and public health interventions, for research and for consumer education. Future efforts will focus on estimating the number of food-borne hospitalizations and deaths, the economic cost of food-borne illness and the burden of water-borne illness in order to provide crucial information to support research, policy and action.

Introduction

The Public Health Agency of Canada (the Agency) estimates that each year about 1 in 8 Canadians (4 million people) get sick from the food they eat (1). The results of a 2013 study show that four pathogens cause about 90% of the 1.6 million illnesses caused by known pathogens: *Norovirus* (1 million cases), *Clostridium perfringens* (177,000 cases), *Campylobacter* (145,000 cases) and nontyphoidal *Salmonella* (88,000 cases). This work represents collaboration between the Enteric Surveillance and Population Studies Division of the Centre for Food-borne, Environmental and Zoonotic Infectious Diseases and the Laboratory for Food-borne Zoonoses within the Agency. These estimates draw extensively from Canada's multiple complementary disease surveillance systems, which are crucial to the development of reliable estimates of the burden of food-borne illness as well as from peer-reviewed literature. Such estimates are useful for decision-makers developing food safety interventions, public health professionals designing consumer education campaigns and, to inform future work, for researchers. This report will detail how these burden of illness estimates were calculated and describe future research plans to better inform efforts to reduce this considerable burden of illness to Canadians.

How the estimates were calculated

The Canadian burden of illness estimates are based extensively on data from four disease surveillance systems. The Canadian Notifiable Disease Surveillance System and the National Enteric Surveillance Program provided data on laboratory-confirmed cases for select pathogens. The National Studies on Acute Gastrointestinal Illness (NSAGI) includes population-based studies on the magnitude, distribution and burden of acute gastrointestinal illness (AGI) in Canada. Finally, FoodNet Canada is a sentinel site surveillance system that provides information on infectious gastrointestinal cases, clinical features, risk factors and sources of exposure. **Table 1** gives a summary of the systems that contributed to the calculation of the burden of food-borne illness estimates.

Table 1: Summary of Canadian surveillance databases used in the burden of food-borne illness estimates

Surveillance database	Main functions	Role in estimating the annual burden of food-borne illness	Timeframe of data used
<u>Canadian Notifiable Disease Surveillance System</u> (2)	National database of laboratory-confirmed illnesses for select pathogens	Provided total annual numbers of laboratory-confirmed cases.	2000-2008
<u>National Enteric Surveillance Program</u> (3)	Aggregate counts of laboratory-confirmed cases from provincial laboratories for select pathogens	Provided total annual numbers of laboratory-confirmed cases.	2000-2010
<u>National Studies on Acute Gastrointestinal Illness</u> (4)	Population studies explore the magnitude, distribution and burden of acute gastrointestinal illness in Canada.	Provided information on care-seeking and stool submission behaviour to inform under-diagnosis multipliers.	2001-2002, 2002-2003 and 2005-2006
<u>FoodNet Canada</u> (5)	Sentinel site surveillance system that provides information on both cases of infectious gastrointestinal illness and sources of exposure within defined communities. Provides information on clinical features and risk factors.	Contributed information on pathogen-specific severity of symptoms (i.e. presence of blood in diarrhea and the duration of diarrhea) and travel-related illnesses.	2005-2010

Note: Though PulseNet Canada (6) and the Canadian Integrated Program for Antimicrobial Resistance Surveillance (7) were not used in developing these estimates they are other important surveillance systems for food-borne illness in Canada.

Specified pathogens

Estimates of the burden of food-borne illness are available for 30 specific pathogens. For some of these pathogens, such as *Salmonella* and *Campylobacter*, laboratory-confirmed cases are reported in our surveillance systems. For these pathogens the numbers of reported cases were adjusted for under-reporting and under-diagnosis. To do this, pathogen-specific multipliers were estimated to extrapolate the likely number of cases at the population level, by taking into account such factors as the probability that an affected individual will seek medical care and be tested, and the likelihood of a positive sample being reported to national surveillance. For example, for every case of *Salmonella* reported to national surveillance, it is estimated that there are about 26 cases occurring in the community. The complete parameters used to construct these multipliers can be found in the technical appendix accompanying the published report.

For other specified pathogens that are not adequately captured as part of Canadian laboratory-confirmed surveillance systems, such as norovirus or *Clostridium perfringens*, symptom-based models were applied to national data on the incidence of gastrointestinal illness to estimate the number of domestically acquired, food-borne cases occurring at the community level.

All of these initial estimates for specified pathogens were then further adjusted for the proportions that were likely to be travel-related and food-borne, in order to generate estimates of the annual burden of domestically acquired food-borne illnesses. For example, for *Salmonella* cases, 26% of illness is estimated to be travel-related, and 80% of domestic illness is estimated to be acquired through the food-borne route (as opposed to exposure through person-to-person contact, water, animals, etc.).

Unspecified agents

Of the 4 million cases of food-borne illness, in only 1.6 million are the pathogens specified; the remaining 2.4 million are unspecified. These illnesses include those caused by known agents with insufficient data, undiscovered agents and unrecognized food-borne agents. To estimate the burden related to unspecified agents, data from the NSAGI population surveys were used to estimate the annual incidence of AGI in the Canadian population. The number of cases attributed to the 25 specified pathogens that are known to cause symptoms of AGI were subtracted from this national total (5 of the 30 known pathogens were excluded as they are not known to cause symptoms of AGI). The residual number of AGI cases was assumed to be caused by unspecified pathogens. This estimate was then adjusted for the proportions that were likely to be travel-related and food-borne, based on estimated proportions for the 25 known pathogens causing AGI.

Discussion

The knowledge that every year 4 million Canadians get sick from 30 food-borne pathogens (1.6 million) and unspecified agents (2.4 million) adds to the understanding of the burden of food-borne illness in Canada. Estimates of this burden are important tools for planning and implementing programs to reduce such illnesses and can also help to inform consumer education campaigns as well as research.

The pathogen-specific findings from this study show a similar ranking of pathogens to those reported by international food-borne illness estimation efforts (United States (8,9), the Netherlands (10), Australia (11), New Zealand (12) and France (13)), though each country has employed slightly different methods based on different available data sources. For example, in the United States it is estimated that the same four major pathogens (*Norovirus*, *Clostridium perfringens*, *Campylobacter*, nontyphoidal *Salmonella* spp.) cause approximately 88% of food-borne illnesses (8). The similarity of the results validates the accuracy of the current Canadian estimates.

Future work related to this initiative being led by the Agency includes generating estimates for the annual number of hospitalizations and deaths related to food-borne illness, and estimating the economic costs to Canada of the illnesses associated with these same 30 pathogens and unspecified agents. In addition, the Agency is leading efforts to estimate the burden of water-borne illness and is currently implementing an expert elicitation process to further inform our understanding of the dominant routes of transmission for key enteric pathogens in Canada.

Conclusion

Canada is fortunate to have a large supply of valuable surveillance and population study data to support burden of illness initiatives. This is only possible with broad collaboration among the provinces and territories across Canada. The estimates of the burden of food-borne illness provide crucial information to support research, policy and action. Future work will help to further our understanding of food-borne illness and interventions to prevent it.

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Conflict of Interest

No conflicts of interest to declare.

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Summary: *Weight of evidence* – Factors to consider when investigating a food-borne illness outbreak

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Introduction

A guidance document, *Weight of Evidence: Factors to Consider for Appropriate and Timely Action in a Food-borne Illness Outbreak Investigation* (1), was developed to assist federal government decision-makers weigh the scientific evidence collected during a food-borne illness outbreak investigation in order to inform risk mitigation actions.

The objective of the document is to provide guidance on how to weigh evidence collected during epidemiologic, laboratory and food safety investigations in a food-borne illness outbreak investigation, as part of an overall health risk assessment process carried out by Health Canada. This is a short summary of the document.

Approach

This document was collaboratively developed by Health Canada, the Public Health Agency of Canada and the Canadian Food Inspection Agency, in accordance with a recommendation made in the 2009 Weatherill Report (2). Standardized criteria were established to weigh epidemiologic, laboratory and food safety evidence collected during a food-borne illness outbreak investigation. Factors to consider were outlined, and guidance on how much weight to assign the evidence for each criterion was agreed upon.

Highlights

Table 1 outlines the key aspects of each chapter in the weight of evidence guidance document.

Table 1: Highlights of the weight of evidence guidance document

Chapter/section	Highlights
Introduction	Food-borne illness outbreak investigations are complex and multidisciplinary, involving the collection of data from laboratory, food safety and epidemiologic investigations. As data and detailed information are collected, the situation is updated, providing strength to the weight of evidence for risk mitigation action.
Section A: Intact and non-intact sample information	During food-borne illness outbreak investigations, samples of food that may have been eaten by the ill individual(s) are often collected. Samples from opened packages are collected for testing when samples from an intact package are unavailable. In these instances, post-packaging contamination needs to be considered.
Section B: Isolate match	Food samples consumed by the ill people are tested for the presence of food-borne pathogens and are compared with the pathogens that have been isolated from the ill people. Comparisons between isolates are often performed through molecular-typing techniques, such as pulsed-field gel electrophoresis. Four criteria to consider when assessing the strength of microbiological evidence in a food-borne illness outbreak investigation are listed.

Chapter/section	Highlights
Section C: Summary of epidemiologic evidence	Direct and supportive epidemiologic evidence is collected throughout a food-borne illness investigation. While the gold standard epidemiologic evidence would arise from a well-designed analytical study, there are other situations in which the weight of evidence would be considered sufficiently strong to warrant regulatory action based on the epidemiologic evidence alone. Nine criteria to consider when assessing the strength of the epidemiologic evidence in a food-borne illness outbreak investigation are listed.
Section D: Traceback and traceforward	Once a food has been linked to cases of illness, food safety investigators attempt to determine from where the food originated (traceback) and/or other places to which the food was distributed (traceforward) in order to help inform a risk management decision. Five situations are presented to be used as a guide in obtaining the weight of evidence needed to issue a recall and/or other risk management action(s), to ensure that all contaminated product is identified and that the source of contamination is found.
Section E: Health risk assessment	Health risk assessments for microbiological hazards are requested by Canadian Food Inspection Agency technical assessors and/or by provinces and territories, and are performed by Health Canada for food-borne illness outbreak situations. A scientific evaluation team at Health Canada assesses data collected through the laboratory, food safety and epidemiologic investigations and assigns a health risk based on the information that is available at the time of the risk assessment request.
Section F: Health risk definitions	The level of health risk is determined by taking the hazard identification, the exposure assessment and the hazard characterization into account. Definitions for the three health risk categories are provided.
Section G: Potential risk management actions after a health risk assessment	A number of risk management actions can be undertaken following a health risk assessment. The type of action taken will depend on the level of the health risk and other factors.
Section H: Scenario examples	Case studies are provided to demonstrate how the weight of evidence is considered for action in a food-borne illness outbreak investigation. The case studies are provided for guidance only.

Results

The totality of epidemiologic, laboratory and food safety evidence is evaluated through a health risk assessment, and a health risk level is assigned to the food in question. The weight of evidence guidance document has played a central role in the conduct of health risk assessments, thereby facilitating timely and appropriate risk mitigation action. The document is currently undergoing a process of review, led by Health Canada, and this is scheduled for completion in 2014.

Conclusion

The use of a guidance document with standardized criteria to assess the weight of evidence in food-borne illness outbreak investigations facilitates the timely completion of health risk assessments of suspect food vehicles and informs the implementation of public health actions to mitigate food-borne risks to consumers.

Conflict of interest

No conflicts of interests to declare.

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Summary: Canada's *Food-borne Illness Outbreak Response Protocol*

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Abstract

Background: The burden of illness due to food-borne pathogens each year in Canada is significant. Investigations of food-borne illness outbreaks, particularly those with cases in more than one jurisdiction, are complex. Accordingly, efficient outbreak response requires the coordination and collaboration of many investigative partners.

Objective: To highlight the Public Health Agency of Canada's *Food-borne Illness Outbreak Response Protocol* (FIORP), the primary guidance document for investigations of multi-jurisdictional food-borne illness outbreaks in Canada.

Approach: The current version of the FIORP was developed in 2010 by the Public Health Agency of Canada following consultation with Health Canada, the Canadian Food Inspection Agency, and provincial and territorial stakeholders.

Results: The FIORP outlines guiding principles and operating procedures to enhance collaboration and coordination among multiple investigative partners in response to multi-jurisdictional food-borne illness outbreaks. It has provided guidance for the conduct of 22 such investigations led by the Public Health Agency of Canada's Centre for Food-borne, Environmental and Zoonotic Infectious Diseases between 2011 and 2013. Furthermore, it has also served as a guide for the development of provincial protocols.

Conclusion: The timely and effective investigation of and response to multi-jurisdictional food-borne illness outbreaks in Canada is facilitated and enhanced by the FIORP.

Introduction

The causes of food-borne illness are varied and may include a host of viruses, bacteria, parasites and toxins. Food-borne pathogens account for approximately 4 million episodes of illness in Canadians each year (1), ranging from mild illness to significant morbidity with long-term sequelae or death. The economic impact of food-borne illness in Canada is also substantial and has been estimated at almost \$1.1 billion for every 1 million annual cases of acute bacterial food-borne illness alone (2).

The investigation of and response to food-borne illness outbreaks with cases in more than one province or territory, or in Canada and another country, is a complex undertaking, requiring the involvement of multiple departments from different levels of government. The primary document for guiding the collaborative efforts required in a multi-jurisdictional food-borne illness outbreak investigation in Canada is the *Food-borne Illness Outbreak Response Protocol* (FIORP) (3).

Given the high profile of food-borne illness outbreaks in Canada, and the ongoing relevance and central role of the FIORP in such investigations, the present article will provide a summary of the Protocol's main features,

including its purpose and guiding principles, stakeholder roles and responsibilities, and investigation operating procedures.

Approach

The FIORP was first developed in 1999 and was subsequently revised in 2006 to incorporate the role of the Public Health Agency of Canada after the Agency's creation in 2004. The current FIORP document was updated in 2010 following a consultative process with federal/provincial/territorial stakeholders, including the Council of Chief Medical Officers of Health and the Federal/Provincial/Territorial Deputy Ministers of Health.

Protocol

Food safety and public health are areas of shared jurisdiction among all levels of government in Canada. As a result, the identification of and response to multi-jurisdictional food-borne illness outbreaks requires active collaboration among a large number of players. The FIORP applies to enteric outbreaks in Canada when cases are reported in more than one province or territory, or in Canada and another country, and multiple agencies are involved. The scope of the FIORP includes determining the potential existence for a multi-jurisdictional food-borne illness outbreak through to the post-outbreak review process.

The objectives of the FIORP are to enhance collaboration and coordination among partners, establish clear lines of communication, and improve the efficiency and effectiveness of the outbreak response. To meet these objectives, the FIORP delineates the roles and responsibilities of investigative partners (**Table 1**) and provides detailed operating procedures for coordinating the response to a potential multi-jurisdictional food-borne illness outbreak. While the FIORP serves to guide the collaboration of partners in the identification of and response to such outbreaks, including guidance on notification of partners, communication and information-sharing, it does not provide detailed instructions for the conduct of an outbreak investigation. The FIORP can also be used as a model for provinces and territories to develop their own food-borne illness outbreak response protocols when multiple jurisdictions or organizations within a single province or territory are involved.

Table 1: Roles and responsibilities of investigative partners during a multi-jurisdictional food-borne illness outbreak

Investigative partner	Role	Responsibility
Local/regional public health officials	Investigate cases of human enteric illness. Conduct inspections and implement control measures to reduce health risks related to food.	Report cases of enteric illness and food safety investigation findings to provincial/territorial public health officials.
Provincial/territorial public health officials	Conduct provincial/territorial surveillance of enteric illnesses. Validate and coordinate the exchange of epidemiologic data between local/regional and federal public health officials. Conduct laboratory analyses of clinical, food and environmental samples collected in respective jurisdictions.	Report cases of enteric illness and results of laboratory analyses to federal public health officials.

Investigative partner	Role	Responsibility
Provincial/territorial agriculture officials	Conduct food safety investigation at facilities that are not the regulatory responsibility of the Canadian Food Inspection Agency. Implement measures to control the potential source of enteric illnesses.	Report investigation findings and actions to investigative partners.
Public Health Agency of Canada	Conduct national surveillance of enteric illnesses. Conduct centralized analysis of epidemiologic data. Assess the weight of epidemiologic evidence for action. Conduct laboratory analyses and provide laboratory reference services for strain identification and characterization of clinical, food and environmental samples. Lead and coordinate public communications.	Lead and coordinate the response to multi-jurisdictional outbreaks.
Canadian Food Inspection Agency	Conduct food safety investigation, including inspection activities. Coordinate food recalls and other measures to control the potential source of illnesses. Provide laboratory analysis of food samples.	Report investigation findings and actions to investigative partners.
Health Canada	Conduct a health risk assessment of the implicated source(s) of illnesses. Develop health policies and standards based on investigation findings, when applicable.	Assign a health risk to the implicated source(s) of the illnesses.

A guiding principle of the FIORP is that an Outbreak Investigation Coordinating Committee serves as the main forum for sharing and interpreting information in an outbreak investigation. The Committee comprises representatives designated to act on behalf of the partners from the different departments and levels of government involved in a given outbreak investigation. These representatives may be from the Public Health Agency of Canada, Health Canada, the Canadian Food Inspection Agency, provincial/territorial public health and agricultural departments, or local public health units. Expertise from other agencies, such as those involved in emergency response or the Royal Canadian Mounted Police, is sought as needed. Representation on an Outbreak Investigation Coordinating Committee includes those with expertise in epidemiology, microbiology, food safety and communications.

The main objectives of an Outbreak Investigation Coordinating Committee are to facilitate communication among participating agencies, to serve as a central point to share information from all sources, to discuss outbreak investigation findings, and to achieve consensus on investigation direction and public health action. Any partner in an outbreak situation may request that such a Committee be activated. The Centre for Food-borne, Environmental and Zoonotic Infectious Diseases at the Public Health Agency of Canada is responsible for the coordination of the Outbreak Investigation Coordinating Committee and is considered the lead organization. However, in exceptional circumstances, when a multi-jurisdictional outbreak has occurred predominantly in one province or territory and

that jurisdiction has already established an investigation team, upon the agreement of all Outbreak Investigation Coordinating Committee representatives that province or territory may assume the lead of the Committee.

Each federal/provincial/territorial partner that could be engaged in a nationally led Outbreak Investigation Coordinating Committee has an appointed primary designated representative, known as a FIORP duty officer. Upon activation of the Committee, the Committee lead is responsible for contacting all FIORP duty officers to inform them that the Committee has been established and to ensure that they receive summaries of its activities and actions. FIORP duty officers, in turn, are responsible for the participation of their jurisdiction in the Committee, as required, and notifying and providing regular updates to senior officials within their organization.

Another guiding principle central to the FIORP is that laboratory, epidemiologic or food safety evidence is used to establish the association between illness and a particular food as the source of an outbreak. The Public Health Agency of Canada, as the Outbreak Investigation Coordinating Committee lead, is responsible for coordinating the epidemiologic investigations of food-borne illness outbreaks, including the overall collation and analyses of epidemiologic data, in collaboration with the affected partners. Food safety investigations are undertaken by the Canadian Food Inspection Agency or the appropriate regulatory officials within the affected jurisdiction. Each partner is responsible for conducting appropriate laboratory testing of clinical and food samples, and sharing the results for discussion with the Committee.

Although the Public Health Agency of Canada leads and coordinates public communications, each Outbreak Investigation Coordinating Committee partner also has responsibility for public communications within its respective jurisdiction. Communications staff and content experts in the Committee work together to develop products to provide updates to the public, the media and other stakeholders, as required, according to risk communications principles. Communication activities are coordinated among Committee partners to achieve consistent and complementary messaging across involved jurisdictions.

Health Canada is responsible for carrying out a health risk assessment of a food that is suspected of being the source of an outbreak. Epidemiologic, microbiologic and food safety data are considered in the assessment, which in turn determines the level of risk posed by the suspected source/implicated food. Health risk assessment decisions are shared with the Outbreak Investigation Coordinating Committee and are used to inform public health action. Public health and food safety actions to address the source of a food-borne illness outbreak may include issuing a recall, detaining a product, disposing of food, public communication regarding prevention and control measures, case and contact management, and prophylaxis (e.g. vaccination for hepatitis A contacts), as well as the review and enhancement of industry procedures and requirements, and the updating and/or development of new government policies, standards or guidelines.

A new feature of the 2010 FIORP was the addition of the option for any partner involved in an outbreak response to request a post-outbreak review. Such reviews, generally chaired by the Outbreak Investigation Coordinating Committee lead, provide an opportunity for partners to examine what worked well and what could have been improved in a particular investigation. Committee partners may identify measures to prevent recurrence, such as new or revised policies or standards; assess the need for further scientific studies; develop improved practices for future investigations; and recommend improvements or adjustments to the FIORP.

Since being revised in 2010, the FIORP has served as the guiding protocol for 22 Outbreak Investigation Coordinating Committees led by the Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada, between 2011 and 2013. These outbreak investigations have involved both domestic and international partners, and implicated pathogens have included *E. coli*, *Salmonella*, *Listeria*, *Cyclospora* and hepatitis A. The FIORP is currently undergoing review, and a revised version will be developed. The Public Health Agency of Canada, as the custodian of the FIORP, will oversee this process through collaborative engagement of key partners and incorporation of recommendations received through post-outbreak reviews.

Conclusion

The FIORP plays an essential role in the effective investigation of and response to multi-jurisdictional food-borne illness outbreaks in Canada. Scheduled review of its provisions ensures that it can adapt to changing realities and provides a means to incorporate post-outbreak recommendations and lessons learned.

Conflict of interest

There are no conflicts of interest to declare.

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